MAJOR ARTICLE

Prevalence and Evolution of Renal Impairment in People Living With HIV in Rural Tanzania

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Background. We assessed the prevalence, incidence, and predictors of renal impairment among people living with HIV (PLWHIV) in rural Tanzania.

Methods. In a cohort of PLWHIV aged ≥15 years enrolled from January 2013 to June 2016, we assessed the association between renal impairment (estimated glomerural filtration rate < 90 mL/min/1.73 m^2) at enrollment and during follow-up with demographic and clinical characteristcis using logistic regression and Cox proportional hazards models.

Results. Of 1093 PLWHIV, 172 (15.7%) had renal impairment at enrollment. Of 921 patients with normal renal function at baseline, 117 (12.7%) developed renal impairment during a median follow-up (interquartile range) of 6.2 (0.4–14.7) months. The incidence of renal impairment was 110 cases per 1000 person-years (95% confidence interval [CI], 92–132). At enrollment, logistic regression identified older age (adjusted odds ratio [aOR], 1.79; 95% CI, 1.52–2.11), hypertension (aOR, 1.84; 95% CI, 1.08–3.15), CD4 count <200 cells/mm^3 (aOR, 1.80; 95% CI, 1.23–2.65), and World Health Organization (WHO) stage III/IV (aOR, 3.00; 95% CI, 1.96–4.58) as risk factors for renal impairment. Cox regression model confirmed older age (adjusted hazard ratio [aHR], 1.85; 95% CI, 1.56–2.20) and CD4 count <200 cells/mm^3 (aHR, 2.05; 95% CI, 1.36–3.09) to be associated with the development of renal impairment.

Conclusions. Our study found a low prevalence of renal impairment among PLWHIV despite high usage of tenofovir and its association with age, hypertension, low CD4 count, and advanced WHO stage. These important and reassuring safety data stress the significance of noncommunicable disease surveillance in aging HIV populations in sub-Saharan Africa.

Keywords. HIV; renal impairment; sub-Saharan Africa.

Widespread use of antiretroviral treatment (ART) has reduced the incidence of opportunistic infections among HIV-infected patients dramatically—hence improving health and life expectancy to near normal [1, 2]. As the HIV-infected population is aging, the causes of morbidity and mortality among HIV-infected patients are shifting from opportunistic infections to noninfectious disorders such as liver, cardiovascular, and kidney diseases [3]. Kidney dysfunction among HIV patients has been reported to be associated with increased morbidity and mortality [4, 5].

In sub-Saharan Africa (SSA) the prevalence of kidney dysfunction in people living with HIV (PLWHIV) has been shown to be high—ranging from 25% to 77% [6–9]. Contributing factors to renal impairment are the high rate of patients with hypertension and diabetes mellitus, as well as co-infections [10] and chronic use of nephrotoxic drugs such as tenofovir disoproxil fumarate (TDF), atazanavir/ritonavir (ATV/r), and lopinavir/ritonavir (LPV/r) [11–13]. TDF is widely used in SSA as a first line ART due to its high efficacy and low side effects and its simultaneous effect against hepatitis B infection [14, 15].

Data on kidney function in PLWHIV from rural SSA regions are scarce, and almost no data in longitudinal cohorts are available. The Kilombero and Ulanga Antiretroviral Cohort (KIULARCO) offers a perfect setting to study prevalence rates and predictors of renal impairment among newly diagnosed PLWHIV and incidence rates of renal impairment during follow-up in a rural SSA setting [16, 17].

METHODS

Study Design

We conducted a prospective cohort study among HIV-infected patients attending the Chronic Diseases Clinic of Ifakara (CDCI) at the Saint Francis Referral Hospital in Ifakara. All patients attending the CDCI were invited to participate in the

Kilombero and Ulanga Antiretroviral Cohort (KIULARCO), a cohort established 2005 comprising almost 9000 enrolled patients and around 3500 patients on active follow-up [16, 17]. The CDCI serves the population from 2 different districts in southwestern Tanzania, namely the Kilombero and Ulanga districts in the Morogoro region. According to the last census in 2012, the population of the Kilombero district is 407 880 and that of the Ulanga district is 265 203 [18].

Study Population

All newly diagnosed ART-naïve HIV-infected patients enrolled in KIULARCO between January 2013 and June 2016 who met the following criteria were included in this analysis: age ≥15 years, availability of a serum creatinine measurement at enrollment, at least 1 control creatinine measurement during follow-up, and the availability of a signed informed consent. The last date of follow-up was June 30, 2016.

Laboratory and Clinical Investigations

Demographic, clinical, laboratory, and pharmaceutical data prospectively collected within KIULARCO were extracted from the electronic database. In brief, enrolled patients undergo clinical assessment and baseline investigations on the same day. The baseline laboratory investigations include CD4 T-cell count (BD FACS Calibur, Franklin Lakes, NJ), complete blood cell count, aspartate aminotransferase, and alanine aminotransferase. Serum creatinine was measured using the Cobas c 111 Analyzer (Roche Diagnostics, Rotkreuz, Switzerland), which uses absorption photometry to determine the amount of absorbance and uses it to calculate the concentration in the sample solution. Laboratory examinations are repeated routinely twice a year unless additionally requested upon clinical indication. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Diseases Epidemiology (CKD-EPI) formula with the ethnicity factor included in the calculation. According to "Kidney Disease: Improving Global Outcome" (KDIGO), renal impairment was categorized as either mild (eGFR, 60–89 mL/min/1.73 m^2), moderate (eGFR, 30–59 mL/min/1.73 m^2), or severe (eGFR < 30 mL/min/1.73 m^2) [19].

Blood pressure (BP) was measured at every clinic visit. Hypertension was defined as having a systolic BP of ≥140 mmHg and/or a diastolic BP ≥90 on 2 consecutive visits measured while sitting, having a history of hypertension, or currently taking antihypertensive medications [20].

Body mass index (BMI) was calculated using weight in kilograms divided by the square of the height in meters. It was categorized as underweight (BMI < 18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), and overweight (≥25 kg/m^2) [21].

Tuberculosis (TB) was defined as either having a recorded positive GeneXpert (Cepheid, Sunnyvale, CA) in the sputum or another body fluid sample, or a chest x-ray suggesting tuberculosis together with at least 1 TB symptom, or receiving antituberculosis treatment.

Statistical Analysis

Continuous variables are presented using median and interquartile range (IQR). Categorical variables are presented as frequencies and percentages. The outcome variable of renal impairment was defined as having an eGFR below 90 mL/min/1.73 m^2. We used a logistic regression model to assess the predictors of renal impairment at enrollment.

We performed Cox regression to assess the association between baseline covariates and the development of renal impairment. Patients who had renal impairment at enrollment were excluded from this analysis. Kaplan-Meier estimates were used to describe the cumulative probability of developing renal impairment according to the exposure status and were compared using the log-rank test.

In multivariate analyses, we a priori identified and included potential predictors of renal impairment; age, sex, BMI, HIV World Health Organization (WHO) stage, CD4 counts, hypertension, ART use, and TB diagnosis.

All analyses were done with Stata, version 14 (Stat Corp, College Station, TX).

Ethics Statement

All study participants provided written informed consent at enrollment in KIULARCO. Ethical approval was obtained from the Ifakara Health Institute review board, the National Health Research Committee of the National Institute of Medical Research of Tanzania, the Tanzania Commission of Science and Technology, and the Ethikkomission Nordwest und Zentralschweiz (EKNZ; Switzerland).

RESULTS

A total of 2267 patients were enrolled in KIULARCO from January 2013 to June 2016. A total of 1093 (48.2%) patients could be included in this analysis, and 1174 (51.58%) were excluded for the following reasons: 388 (17.1%) were already on ART, 284 (12.5%) did not have serum creatinine measurement at enrollment, 392 (17.3%) did not have at least 1 control creatinine measurement during follow-up, and 110 (4.8%) were younger than age 15 years at enrollment (Figure 1). We did not find any difference between patients without and those with a creatinine measurement (Supplementary Table 1).

Baseline demographic and clinical characteristics of all patients are summarized in Table 1. Overall, 66% of patients were female, median age (IQR) was 39 (32.3–47.0) years. Median BMI (IQR) was 20.9 (18.9–23.4) kg/m^2; of these, 21.5%, 60.7%, and 16.4% were underweight, normal weight, and overweight, respectively. The median CD4 count (IQR) was 207 (77–378) cells/mm^3, with 47.8% of patients presenting with a CD4 count of <200 cells/mm^3. An advanced HIV disease stage (WHO stage III or IV) at enrollment was present in 45.4% of patients. A total of 196 patients (17.9%) were diagnosed with TB, and 114 patients (10.4%) were diagnosed with hypertension at enrollment.
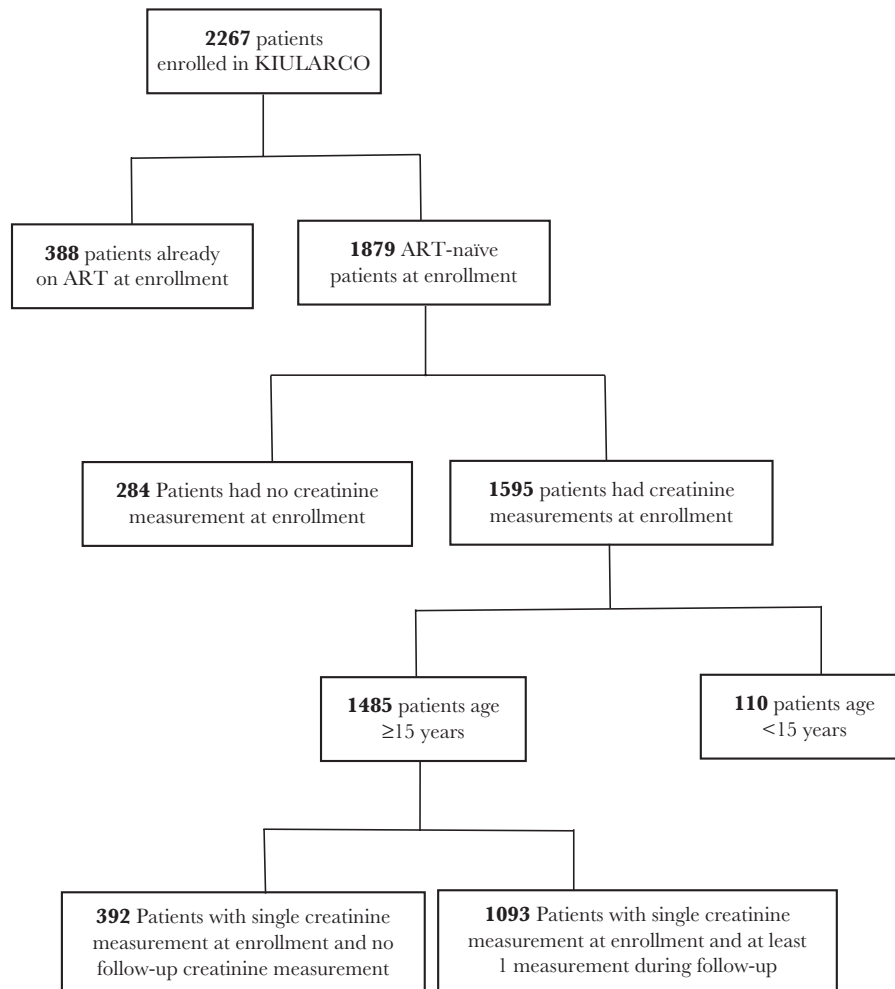
Figure 1. Patients' flow chart.

Among the 999 (91.2%) patients who started ART, median time from enrollment to start of therapy (IQR) was 14 (6–35) days. The majority of these patients (676, 61.9%) started ART with a single tablet combination of tenofovir disoproxil fumarate (TDF), lamivudine (3TC), and efavirenz (EFV), followed by 251 patients (23.0%) on a single tablet combination of TDF, emtricitabine (FTC), and EFV. Additionally, there were 33 patients (3.0%) who had moderate or severe renal impairment (eGFR < 60 mL/min/1.73 m^2) at enrollment, but they were still prescribed a TDF-based regimen. Patients who started ART with non-TDF-based regimens (n = 68 [6.2%] had a lower median eGFR at enrollment compared with those with TDF-based regimens (median eGFR, 105.7 vs 128.3 mL/min/1.73 m^2; $P < .001$).

At the end of the study period, 773 patients (70.7%) were still under active follow-up, 183 patients (16.7%) were lost to follow-up, 62 patients (5.7%) had died, and 75 patients (6.9%) had been transferred to other health facilities. The median length of follow-up among those who had normal kidney function at enrollment (IQR) was 6.2 (0.4–14.7) months compared with 2.0 (0.2–8.8) months in those with renal impairment ($P < .001$).

Predictors of Renal Impairment at Enrollment

Median eGFR at enrollment (IQR) was 126.8 (104.8–140.1) mL/min/1.73 m^2, and 15.7% (172/1093) had renal impairment, defined as eGFR <90 mL/min/1.73 m^2. Among patients with renal impairment, 9.1%, 3.9%, and 2.7% had mild, moderate, and severe renal impairment, respectively. Among 172 patients who had renal impairment at enrollment, 129 (75%) had improved renal function during follow-up visits to eGFR above 90 mL/min/1.73 m^2. The median time to normalize renal function (IQR) was 6.8 (2.3–15.4) months.

In the logistic regression model to determine independent predictors of renal impairment at enrollment, the multivariable analysis (Table 2) showed a significant association between renal impairment and older age (per 10-year increase), with an adjusted odd ratio (aOR) of 1.79 (95% confidence interval [95% CI], 1.52–2.11; $P < .001$). Furthermore, patients who were diagnosed with hypertension at enrollment had almost twice the risk

Table 1. Baseline Characteristics of the Patients Involved in the Study

	Total Cohort (n = 1093)	Renal Impairment at Baseline (eGFR < 90) (n = 172)	Normal Renal Function at Baseline (n = 921)	Normal Renal Function During Follow-up (n = 804)	Renal Impairment During Follow-up (eGFR < 90) (n = 117)
Sex, No. (%)					
Male	376 (34.4)	69 (40.1)	307 (33.3)	264 (32.8)	43 (36.7)
Female	717 (65.6)	103 (59.9)	614 (66.7)	540 (67.2)	74 (63.3)
Age, median (IQR), y	39.0 (32.3–47.0)	46.2 (38.9–55.8)	37.9 (31.6–45.6)	37.3 (31.3–44.3)	45.6 (36.2–54.3)
WHO stage, No. (%)					
I	417 (38.2)	26 (15.1)	391 (42.5)	351 (43.7)	40 (34.2)
II	159 (14.6)	21 (12.2)	138 (15.0)	122 (15.2)	16 (13.7)
III	327 (29.9)	73 (42.4)	254 (27.6)	221 (27.5)	33 (28.2)
IV	169 (15.5)	46 (26.7)	123 (13.4)	95 (11.8)	28 (23.9)
BMI					
Median (IQR), kg/m^2	20.9 (18.9–23.4)	20.6 (18.3–23.4)	20.9 (18.9–23.4)	21.0 (19.0–23.6)	19.9 (18.1–22.6)
<18.5, No. (%)	235 (21.5)	45 (26.2)	190 (20.6)	158 (19.7)	32 (27.4)
≥18.5–24.9, No. (%)	663 (60.7)	97 (56.4)	566 (61.5)	496 (61.7)	70 (59.8)
≥25, No. (%)	179 (16.4)	27 (15.7)	152 (16.5)	139 (17.3)	13 (11.1)
CD4 count					
Median (IQR), cells/mm^3	207 (77–378)	125 (48–267)	221 (87–393)	229 (93–402)	146 (48–311)
<200, No. (%)	522 (47.8)	106 (61.6)	416 (45.2)	344 (42.8)	72 (61.5)
≥200, No. (%)	549 (50.2)	61 (35.5)	488 (53.0)	443 (55.1)	45 (38.5)
CD4					
Median (IQR), %	11 (5.0–19.0)	7.4 (4.0–14.5)	12.0 (6.0–20.0)	12.1 (6.0–20.0)	8 (4.0–17.0)
Tuberculosis, No. (%)					
Yes	196 (17.9)	46 (26.7)	150 (16.3)	134 (16.7)	16 (13.7)
No	875 (80.1)	124 (72.1)	751 (81.5)	652 (81.1)	99 (84.6)
Hypertension, No. (%)					
Yes	114 (10.4)	26 (15.1)	88 (9.6)	71 (8.8)	17 (14.5)
No	962 (88.0)	140 (81.4)	822 (89.3)	724 (90.1)	98 (83.8)
First ART started, No. (%)					
AZT+3TC+NVP	11 (1.0)	3 (1.7)	8 (0.9)	8 (1.0)	0
AZT+3TC+EFV	40 (3.7)	13 (7.6)	27 (3.18)	24 (3.0)	3 (2.6)
TDF+FTC+EFV	251 (23.0)	24 (14.0)	227 (26.7)	193 (24.0)	34 (29.1)
TDF+FTC+NVP	1 (0.1)	0	1 (0.12)	0	1 (0.9)
TDF+3TC+EFV	676 (61.9)	94 (54.7)	582 (63.2)	514 (63.9)	68 (58.1)
ABC+3TC+EFV	16 (1.5)	14 (8.1)	2 (0.2)	0	2 (1.7)
TDF/FTC/LPV/r	1 (0.1)	0	1 (0.1)	1 (0.1)	0
AZT+3TC+LPV/r	1 (0.1)	1 (0.6)	0	0	0
TDF+FTC+ATV/r	2 (0.2)	0	2 (0.2)	1 (0.1)	1 (0.9)
Time under observation					
Median (IQR), mo			6.2 (0.4–14.7)	12.8 (6.2–21.9)	5.7 (1.8–9.2)

We had 93.2% of patients starting on a TDF-based regimen, 2 patients on an LPV/r regimen, and 2 patients on ATV/r.

Abbreviations: 3TC, lamivudine; ABC, abacavir; ART, antiretroviral treatment; ATV/r, atazanavir/ritonavir; AZT, zidovudine; BMI, body mass index; EFV, efavirenz; eGFR, estimated glomerular filtration rate; FTC, emtricitabine; IQR, interquartile range; LPV/r, lopinavir/ritonavir; LTFU, loss to the follow-up; NVP, nevirapine; TDF, tenofovir disoproxil fumarate; WHO, World Health Organization.

of having renal impairment compared with those who were non-hypertensive (aOR, 1.84; 95% CI, 1.08–3.15; P = .026). A CD4 count <200 cells/mm^3 (aOR, 1.80; 95% CI, 1.23–2.65; P = .003) and advanced HIV disease (WHO stage III/IV; aOR, 3.00; 95% CI, 1.96–4.58; P < .001) were also associated with renal impairment. We did not find any association with sex, BMI, or TB.

Renal Impairment During Follow-up

Figure 2 shows the plotted evolution of eGFR over time of all the patients who were enrolled in our study. There was a significant improvement in eGFR during the follow-up visits (P < .001). In 117 patients (12.7%), kidney function worsened (−53. 7 mL/min/1.73 m^2; IQR, −77 to −29.6) within a median follow-up (IQR) of 5.7 (1.8–9.2) months. Total time at risk was 1062 person-years, and the incidence of renal impairment was 110 cases per 1000 person-years (95% CI, 92–132). Among these patients, 8.5%, 2.3%, and 2.0% had mild, moderate, and severe renal impairment, respectively. The incidence rate for developing moderate and severe renal impairment was 37 cases per 1000 person-years, (95% CI, 27–50).

Table 2. Univariate and Multivariate Logistic Regression Model for Predictors of Renal Impairment at Baseline

Variable	Univariate Model Unadjusted OR (95% CI)	P Value	Multivariate Model Adjusted OR (95% CI)	P Value
Age, per 10 y	1.81 (1.56–2.09)	<.001	1.79 (1.52–2.11)	<.001
Female sex	0.75 (0.53–1.04)	.086	1.22 (0.83–1.80)	.313
BMI, kg/m²				
≥18.5	1		1	
<18.5	1.37 (0.94–2.00)	.100	0.82 (0.53–1.27)	.383
CD4 count, cells/mm³				
≥200	1		1	
<200	2.04 (1.45–2.87)	<.001	1.80 (1.23–2.65)	.003
Hypertension				
No	1		1	
Yes	1.73 (1.08–2.78)	.022	1.84 (1.08–3.15)	.026
WHO stage				
I or II	1		1	
III or IV	3.55 (2.47–5.11)	<.001	3.00 (1.96–4.58)	<.001
Tuberculosis diagnosis				
No	1		1	
Yes	1.86 (1.27–2.72)	.001	1.09 (0.70–1.71)	.691

Abbreviations: BMI, body mass index; CI, confidence interval; OR, odds ratio; WHO, World Health Organization.

The Kaplan-Meier estimates showed that the proportion of patients developing renal impairment was higher among patients older than age 50 years (compared with those aged 50 years and younger: 28.5 vs 9.6%; log-rank $P < .001$), among patients with BMI <18.5 kg/m² (compared with those with BMI ≥ 18.5 kg/m²: 16.8% vs 11.6%; log-rank $P < .041$), and among patients diagnosed with hypertension compared with those without (19.3% vs 11.9%; log-rank $P = .054$). Additionally, the proportion of patients developing renal impairment was higher among patients with WHO stage III/IV compared with WHO stage I/II (16.2% vs 10.6, respectively; log-rank $P = .001$) and those patients with advanced immunosuppression (CD4 < 200 compared with those with CD4 ≥ 200 cells/mm³, 17.3% vs 9.2%, respectively; log-rank $P = .0002$).

Table 3 shows results of Cox regression modeling for risk factors associated with the development of renal impairment during follow-up visits. Factors associated with increased risk of renal impairment in the multivariate analysis included older age (per 10-year increase; adjusted hazard ratio [aHR], 1.85; 95% CI, 1.56–2.20; $P < .001$) and CD4 count <200 cells/mm³ (aHR, 2.05; 95% CI, 1.36–3.09; $P = .001$). Additionally, we found a trend for an association between the development of renal impairment and both WHO stage III/IV (aHR, 1.47; 95% CI, 0.97–2.25; $P = .072$) and TB (aHR, 0.60; 95% CI, 0.34–1.05; $P = .076$). We did not find any association between renal impairment and sex, BMI, hypertension, or use of ART during follow-up. TDF use could not be analyzed as a risk factor as 93.2% of patients received TDF as part of first line treatment.

The final model had a good fit and met the proportional hazard assumption (Schoenfeld's global $P = .521$).

DISCUSSION

In our prospective study among 1093 adult HIV-infected patients in rural Tanzania followed for 1062 person-years, we found a prevalence of renal impairment of 15.7% in treatment-naïve patients. Among patients with normal renal function at enrollment, the incidence rate of developing moderate and severe renal impairment during follow-up was low, with 37 cases per 1000-person years (95% CI, 27–50).

We found a lower prevalence of renal impairment compared with previous studies done in SSA, which documented prevalence ranging from 25% to 77% [6–9]. This could be because in previous studies more patients were diagnosed with advanced HIV disease (WHO stage III or IV and lower CD4 cell counts) compared with our study.

In our study, after adjusting for potential confounders (sex, hypertension, CD4 count, BMI, WHO stage, and TB), age at enrollment (per 10-year increase) remained associated with a 79% higher risk of renal impairment. Likewise, we found that arterial hypertension at enrollment led to almost twice the odds of renal impairment. This is in line with results from a study among HIV patients in Italy [22]. But also, parameters of advanced HIV disease at enrollment (CD4 count < 200 cells/mm³ and WHO stage III or IV) had a higher odds of renal impairment, as previously reported by Mulenga et al. and Gallant et al. [23, 24]. We did not find any association between renal impairment and TB, as reported previously [25].

In contrast, incident renal impairment while on antiretroviral treatment was slightly higher compared with a study done in Spain that found 29 cases per 1000 person-years and was lower compared with another study done in Myanmar that found an incidence rate of 54 cases per 1000 person-years [26, 27]. The wide coverage of ART in HIV patients in SSA and the associated decrease in mortality and increase in patient age has led to an increased risk of developing other comorbidities, such as hypertension, diabetes mellitus, and renal impairment [1–3, 28].

For predictors of renal impairment during follow-up, we performed a Cox proportional hazard model. In the adjusted Cox regression model, we found a strong association between renal impairment and increased age, as well as presenting with low CD4 count at enrollment. These results go in line with a recent study published by Hamzah et al., although they found kidney dysfunction to be more common among patients with white ethnicity compared with other ethnicities [29]. We found a positive association between developing renal impairment and presenting with WHO stage III or IV at enrollment and a negative association between renal impairment and being diagnosed with TB at enrollment, although both factors were not statistically significant. Furthermore, we found that the risk
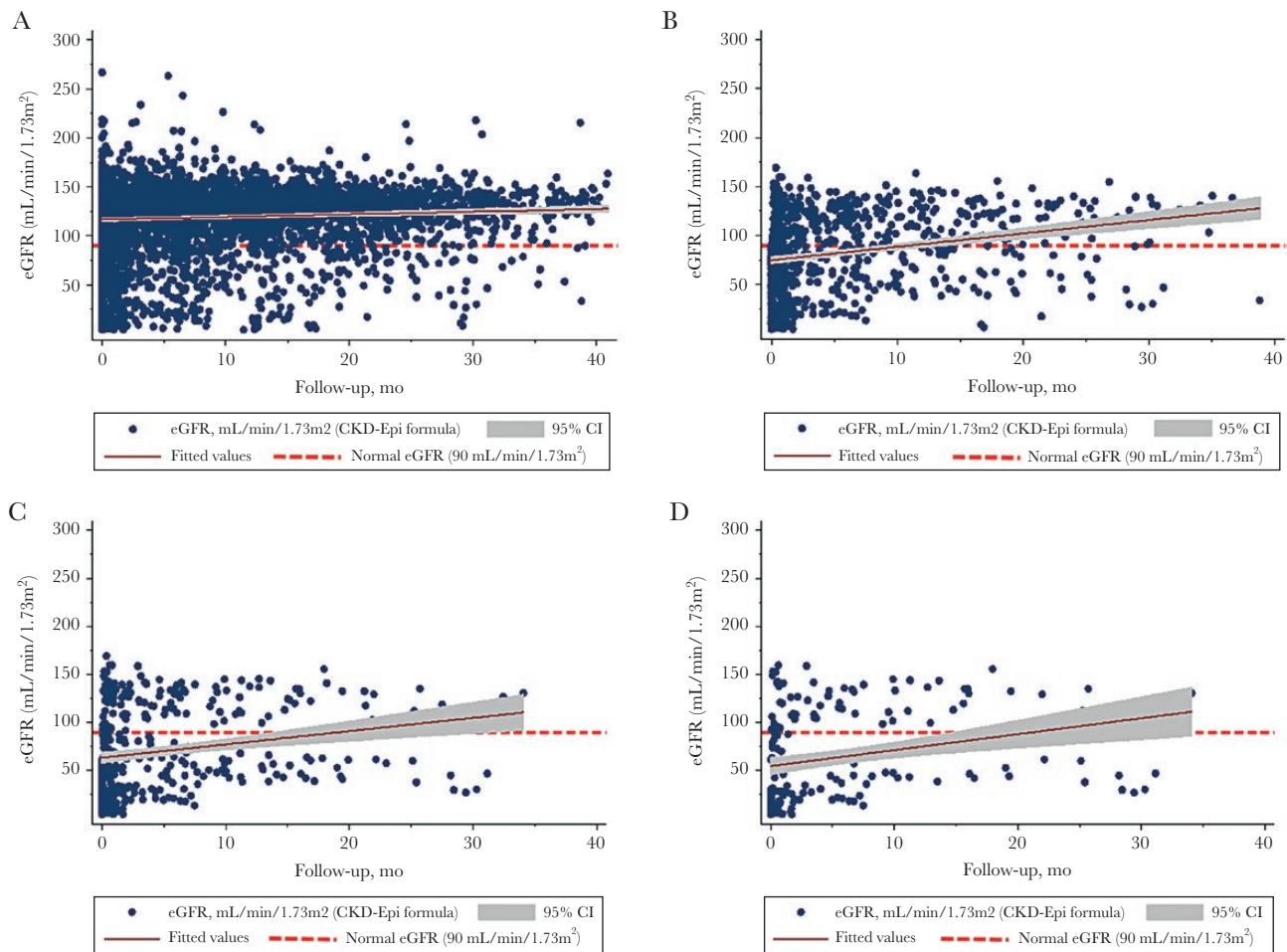
Figure 2. Evolution of eGFR among patients after enrollment. Average evolution of eGFR among patients. A, All patients. B, Patients presented with eGFR <90 mL/min/1.73 m². C, Patients with eGFR <60 mL/min/1.73 m². D, Patients with eGFR <30 mL/min/1.73 m². Abbreviations: eGFR, estimated glomerular filtration rate, CI, confidence interval.

of renal impairment development was 44% lower among those who started ART during follow-up compared with those who did not start, although this was not statistically significant.

Among 29 patients who had severe renal impairment (eGFR < 30 mL/min) at enrollment, kidney function normalized (eGFR ≥ 60 mL/min) during follow-up in 23 patients (79%), 3 patients died, and another 3 patients were lost to follow-up. Additionally, more than 75% of patients who had renal impairment at enrollment normalized within a median time of 6 months; most likely, this was caused by acute kidney injury rather than chronic kidney disease (CKD).

Our study has several limitations. Renal impairment was based on 1 creatinine measurement only; hence we could not differentiate between acute and chronic kidney diseases. We acknowledge it is a common practice to define CKD as having at least 2 eGFR measurements <60 mL/min/1.73 m² more than 3 months apart, but in resource-limited settings, this is a challenge, mainly because transport costs for patients do not allow extra visits [6, 9, 24]. Among the 921 patients with 2 consecutive eGFR measurements available, only 20 (2.2%) developed

at least 2 episodes of eGFR <60 mL/min/1.73 m² during follow-up and only 1 developed CKD. Therefore, our study results should be interpreted with caution as they show loss of kidney dysfunction rather than CKD. Also, in our setting, we do not routinely measure viral load, glycosuria, serum glucose, and proteinuria, which have been reported to be associated with renal impairment [30, 31]. Another possible confounder, for which we did not collect information, is the use of traditional medicines, which according a recent survey done in Tanzania has been shown to be a common practice, involving around 70% of patients with CKD in the community [32]. Similarly, we could not analyze if the renal impairment developed by our patients during follow-up was associated with TDF use as the majority of our patients who started ART (93.2%) also started treatment with a TDF-based regimen. Also, as almost a quarter of our patients presented with a BMI <18.5 kg/m², the calculations of eGFR might have been underestimated. For practicability, we had to decide on 1 formula, despite the fact that this might have been inappropriate for certain subgroups of patients and specific phases of HIV infection.

Table 3. Univariate and Multivariate Cox Proportional Hazards for Predictors of Renal Impairment (With Baseline Covariates) (n = 921)

Variable	Univariate Model Unadjusted HR (95% CI)	P Value	Multivariate Model Adjusted HR (95% CI)	P Value
Age, per 10 y	1.76 (1.50–2.05)	<.001	1.85 (1.56–2.20)	<.001
Female sex	0.83 (0.57–1.21)	.326	1.15 (0.78–1.72)	.483
BMI, kg/m^2				
≥18.5	1		1	
<18.5	1.53 (1.01–2.29)	.043	1.25 (0.81–1.92)	.320
CD4 count, cells/mm^3				
≥200	1			
<200	2.00 (1.38–2.90)	<.001	2.05 (1.36–3.09)	.001
Hypertension				
No	1		1	
Yes	1.65 (0.99–2.76)	.057	1.43 (0.83–2.45)	.193
WHO stage				
I or II	1		1	
III or IV	1.83 (1.27–2.63)	.001	1.47 (0.97–2.25)	.072
Tuberculosis diagnosis				
No	1		1	
Yes	0.94 (0.55–1.59)	.816	0.60 (0.34–1.05)	.076
Started ART				
No	1		1	
Yes	0.83 (0.40–1.70)	.601	0.56 (0.25–1.26)	.159

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; WHO, World Health Organization.

Despite these limitations, we believe that our study has clinical and public health implications due to its prospective study design and comprehensive information on noncommunicable diseases (NCDs), such as hypertension and kidney disease. Awareness of the importance of NCDs in the community is still lacking [33–36], which has been shown in recent survey in Tanzania that reported that only 10.5% of affected persons were aware of an underlying CKD [37]. In most parts of sub-Saharan Africa, NCDs are not routinely screened due to lack of resources, and health care settings are not yet prepared for the management of chronic diseases other than HIV. Additionally, there are very few cohorts in Africa where evaluation of long-term outcomes of chronic diseases can be assessed. According to the Tanzania National Guideline for the Management of HIV and AIDS, screening for NCDs among HIV-infected patients is strongly recommended. However, in reality, unfortunately, this is usually not the practice in most HIV clinics in the country due to lack of reagents and a separation between chronic diseases clinics and HIV clinics. Also, as in most of the HIV clinics nurses are providing ART to the patients, they do not usually perform routine checking of NCDs. A study from Cambodia showed that combining HIV treatment programs with NCD control programs is beneficial [38]. Additionally, most studies in SSA have used Cockcroft-Gault or the Modification of Diet in Renal Diseases equation (MDRD) for calculation of the eGFR instead of the CKD-EPI equation [6, 8, 24]. The CKD-EPI equation is as precise as the MDRD equation in the subgroup of patients with eGFRs lower than 60 mL/min/1.73 m^2; however, it is more accurate in patients with eGFRs above 60 mL/min/1.73 m^2 and is the recommended formula in population screening where CKD status is unknown [39, 40].

CONCLUSION

Our study found a low prevalence of renal impairment among HIV-infected patients despite high usage of TDF and an association of renal impairment with age, hypertension, low CD4 count, and advanced WHO stage. Our results are important and provide reassuring safety data, and they stress the significance of surveillance of noncommunicable diseases such as hypertension in an aging HIV population in SSA. Combining HIV programs with other noncommunicable disease control programs should be the way forward for better outcomes in HIV-infected patients.

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